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A prospective randomized multicenter clinical trial of the Provox2 and Groningen Ultra Low Resistance voice prostheses in the rehabilitation of post-laryngectomy patients: A lifetime and preference study

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SUMMARY

To prospectively study patients' preference for and the lifetime of the Groningen Ultra Low Resistance (GULR) and Provox2 tracheo-esophageal shunt prosthesis (TESP, plural TESPs) in post-laryngectomy patients. Eighty post-laryngectomy patients were included in 4 oncological centers in the Netherlands. We used a repeated measures design study with 4 randomized groups in a partial cross-over design using 3 consecutive TESPs (3 intervals) in different orders. (Group 1: GULR-GULR-GULR; Group 2: GULR-GULR-Provox2; Group 3: Provox2-Provox2-GULR; and Group 4: Provox2- Provox2-Provox2). Replacement dates and reasons for replacement were monitored with questionnaires as were patients' preferences for GULR or Provox2. A great variability of lifetime within and between groups was seen. Mean lifetimes found (all groups and intervals added) were 106.2 and 102.7 days, and median lifetimes were 76 and 65 days for GULR and Provox2, respectively. Lifetime showed no significant differences between groups, intervals, and TESP types. Many patients dropped out due to reasons having to do with GULR-characteristics ($n = 21$). The main dropout reason was "high phonating resistance (HPR)" (57.1%). Only 10 patients preferred GULR. A significantly larger number of patients ($n = 39$, 79.6%) preferred Provox2 either by choice or by dropping out due to GULR-characteristics ($P < 0.001$). The main replacement reasons were "leakage though TESP" (GULR 59.1%, Provox2 52.1%) and HPR (GULR 15.9%, Provox2 12.7%). No significant differences in lifetime between GULR and Provox2 were found. The patients' preference for Provox2 was significant ($P < 0.001$). Patients' preference was a more important outcome measurement in TESP effectiveness than device lifetime.

Introduction

In speech rehabilitation after total laryngectomy, the state-of-the-art method used is the silicone rubber tracheo-esophageal shunt prosthesis (TESP, plural: TESPs). To enable patients to phonate after surgery, a TESP is positioned in the tracheo-esophageal fistula made during the laryngectomy. This TESP has a one-way valve mechanism opening towards the esophagus when the patient exhales while closing off the tracheostoma. This allows the patient to phonate as air passing through the TESP causes vibration of the neopharynx. Several types of TESPs are available.[1,2] In the Netherlands and the rest of Europe, the Provox2 and the Groningen Ultra Low Resistance (GULR) TESPs are the ones most frequently used. Both have a limited lifetime and need to be replaced on a regular basis. Many studies have investigated the lifetime of the different TESPs used nowadays.[3–11] The main reasons for TESP replacement are leakage of fluids through the TESP or an increased airflow resistance during phonation, both caused by biolfilm formation on the TESP surface.[12]

The burden of the replacement on laryngectomees is substantial. The procedure has to be performed in an ENT outpatient clinic and can be uncomfortable.

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A pilot study in our clinic ($n = 20$) showed that the mean GULR lifetime (65 days) was significantly longer than the mean Provox2 lifetime (42 days). The median lifetime for Provox2 and GULR was 40 and 48 days, respectively.[3]

The aim of our study was to compare the Provox2 and GULR TESPs, and evaluate patients' preference for one of these types. We hypothesized that the GULR would have a longer lifetime than the Provox2, that the GULR and Provox2 would otherwise have comparable characteristics (i.e. anterograde replacement method, phonating resistance), and that, due to a longer lifetime, patients would prefer the GULR.

Methods

We performed a multicenter prospective randomized clinical repeated measures trial to study the lifetime of GULR and Provox2. The secondary study parameter was the patients' preference for one of the two TESPs.

Study population

We included 80 laryngectomees aged over 45, with at least 6 months of TESP experience and at least one prior anterograde replacement. Excluded were patients with recurrent carcinoma, no usage of their TESP, or those unfit to undergo anterograde replacement. We included 55 patients at the University Medical Center Groningen (UMCG), 7 at the Radboud University Nijmegen Medical Centre, 13 at the Medisch Centrum Leeuwarden, and 5 patients were included from the VU University Medical Center. The study was approved by the ethical committees in these institutions and all patients gave their informed consent.

Study design

In each subject a follow-up of three consecutive TESPs was carried out. The subjects were randomized into four groups, each with different orders of TESP types (Table 1). In the baseline interval, patients were using their pre-study TESP (GULR or Provox2). Interval 0 was the run-in period, in which patients were getting used to the TESP type used in Interval 1. This ruled out any carry-over effects from their baseline TESP. Interval 1 was the first and Interval 2 was the second intervention period. In Interval 2, Groups 2 and 3 switched to the other TESP type. Post-study preference depicts the patients' TESP type of preference. We chose a repeated measures design to investigate the possible positive effect of using several TESPs of the same type consecutively, in terms of lifetime or users' convenience.

Power analysis was based on the comparison of the mean lifetime of two consecutive equal TESP types in Groups 1 and 4. To detect lifetime difference with an 80% power and a 5% two-sided alpha, and to create a balanced partial cross-over design, each group needed 17 patients. Taking a dropout rate of 15% into account, 80 patients had to be included.

Materials

TESP lifetime was monitored by registering the replacement dates.

Patients' preference for GULR or Provox2 was evaluated by an explorative questionnaire at the end of the study. Moreover we extended this by defining "dropout due to TESP characteristics" as the patient's preference for the other TESP type.

Replacement reasons were carefully monitored by a questionnaire filled out by the physician doing the replacement.

Statistics

First, the randomization was tested by comparing the groups. Mean age was compared with ANOVA. Sex distribution in the groups was compared using the X^2-test. The location of inclusion was divided into "UMCG" and "non-UMCG" in order to evaluate the non-UMCG patients percentages in all groups (X^2-test).

Furthermore, the causes of missing data due to dropout of patients were considered. Some data were in fact missing because we presented the study before all subjects had actually completed the study. We therefore qualitatively evaluated the effects that these missing data might have on our results.

Descriptive statistics were also used on the raw data in order to evaluate the means, medians, and standard deviations of lifetime in days per TESP type per interval. Since lifetime distribution was not normal, we used logarithmically transformed data ("log-lifetimes"). First, we compared the log-lifetime of two types of TESPs in Interval 0, meaning the log-lifetime in Groups 1 and 2 (GULR) compared to the log-lifetime of Groups 3 and 4 (Provox2). The same comparison was made in Interval 1. Continuing in this fashion, the log-lifetimes in Interval 2 were compared using Groups 1 and 3 (GULR) and Groups 2 and 4 (Provox2). All log-lifetime comparisons were made using students' t-test and shown in box plots. In all tests, a $P < 0.05$ was considered significant. All groups then ended up being compared for all intervals using multilevel analysis in order to take into account correlation between measurements within patients.

Finally, to test whether the preference for GULR and Provox2 was the same, we used binomial test, and TESP exchange reasons were evaluated and described.

Results

The following is our data collected in three years and 9 months after the first inclusion. We found no significant differences in mean age between the groups ($P = 0.51$). The sex distribution in our study population is ratio 10:1 (M:F), consistent with the literature.[13–15] However, in Group 3 the sex distribution was 15:5, while in the other groups the sex distribution was 19:1. Nevertheless, no significant relationship between groups and sex was found ($P = 0.08$). Moreover, no relationship between location and group was found ($P = 0.78$).

Table 1
Study design.

Group	*N*	Baseline interval	Interval 0	Interval 1	Interval 2	Post-study preference
1	20	GULR/Provox2	GULR	GULR	GULR	GULR/Provox2
2	20	GULR/Provox2	GULR	GULR	Provox2	GULR/Provox2
3	20	GULR/Provox2	Provox2	Provox2	GULR	GULR/Provox2
4	20	GULR/Provox2	Provox2	Provox2	Provox2	GULR/Provox2

Baseline Interval: interval pre-study.
Interval 0: run-in period, patients are getting used to TESP studied in Interval 1.
Intervals 1 and 2: intervention intervals.
Post-study Preference: TESP of preference of the patient after completing the study.

Table 2 shows the number of completed intervals per group, missing data, and timing of dropout per interval per group. Clearly, many patients ($n = 41$) did not complete the study; this was due to the following reasons. Fourteen patients were included but dropped out before Interval 0 (thus in the pre-study interval). These are displayed in the column labeled "no start" in Interval 0. In Group 1 dropout was due to emigration ($n = 1$), death ($n = 1$), and secondary tumor ($n = 1$). Group 2 lost patients prestart due to death ($n = 2$), no further TESP usage ($n = 1$), and personal reasons ($n = 1$). In Group 3 death occurred once ($n = 1$) prestart. Furthermore, 6 patients (Group 1 ($n = 2$), Group 3 ($n = 2$), and Group 4 ($n = 1$)) did not start in Interval 0 due to reasons that are unclear. In addition 21 patients dropped out due to characteristics of the GULR (explained later); this usually occurred at the moment of TESP exchange. When death or other dropout reasons occurred ($n = 6$) during the intervals, we used this date as the end of the interval. Nine patients were still in the study at the moment of our analysis ("pending"). The timing for all dropouts and "pending" patients are depicted in Table 2.

Lifetime

Table 3 shows the mean and median lifetime of the Provox2 and GULR added per interval, along with all intervals added per TESP type. There is great variability in lifetime within the groups. For example, the standard deviation of GULR lifetime in Interval 0 is larger than the mean lifetime.

Fig. 1 shows lifetime in days in three intervals separated by group. There is great variability between the groups despite the fact that they were expected to be similar (same TESP type).

Looking at the data, there was no normal distribution in all the intervals in terms of lifetime in days; therefore, we used a log transformation on the data. Comparing log-lifetime in Groups 1 and 2 with Groups 3 and 4 in Interval 0 and Interval 1, respectively, no significant difference between these groups was found ($P = 0.64$ and 0.89, respectively). And, although Interval 2 in Group 3 seemed different (i.e. shorter GULR lifetime), when comparing log-lifetime in Groups 1 and 3 with Groups 2 and 4 in Interval 2, no significant difference was actually found ($P = 0.44$).

In addition, using Multilevel Analysis showed no significant difference in lifetime between GURL and Provox2. No beneficial effect for lifetime was shown when patients used the same TESP type consecutively.

Dropout and preference of the patient

Table 4 is a survey of the completed subjects and the patients that dropped out due to GULR-related characteristics. No patients dropped out due to Provox2-related reasons.

Remarkably, many subjects ($n = 21$) using GULR dropped out due to reasons concerning GULR characteristics ("dropout due to GULR"). The most important dropout reason was "high phonating resistance" (HPR) ($n = 12$, 57.1%): some subjects could not produce any sound ($n = 4$) or very little with maximum effort ($n = 5$) directly after the GULR placement. Some patients ($n = 3$) found the GULR phonating resistance in Interval 1 too high and thus dropped out. The second dropout reason was leakage of the GULR directly after insertion ($n = 3$). One of the patients who dropped out due to HPR had also experienced minor direct leakage. Other reasons for dropout were "cleaning problems" ($n = 1$), "increased shortness of breath" in an asthma patient ($n = 1$), "problematic replacement" ($n = 3$), and "sizing problems" ($n = 1$) due to leakage around the TESP; in this latter case, the smallest GULR size was too large (5 mm compared to Provox2 4.5 mm).

When adding the total GULR-related dropout and the number of subjects who ended up with a preference for Provox2, we found a

Table 2
Number of completed intervals per group, missing data, and timing of dropout per interval.

Interval 0						
Group	TESP type	No start	At risk	GULR dropout	Pending	Completed Interval 0
1	GULR	5 (of 20)	15	7	0	8
2	GULR	4 (of 20)	16	2	0	14
3	Provox2	4 (of 20)	16	0	0	16
4	Provox2	1 (of 20)	19	0	1	18
Total		14 (of 80)	66	9	1	56
Interval 1						
Group	TESP type	No start	At risk	GULR dropout	Pending	Completed Interval 1
1	GULR	0	8	1	0	7
2	GULR	0	14	6	0	8
3	Provox2	2[a]	14	0	0	14
4	Provox2	2[b]	16	0	1	15
Total		4	52	7	1	44
Interval 2						
Group	TESP type	No start	At risk	GULR dropout	Pending	Completed study
1	GULR	0	7	0	1	6
2	Provox2	1[c]	7	0	1	6
3	GULR	1[d]	13	5	2	6
4	Provox2	0	15	0	3	12
Total		2	42	5	7	30

TESP type: type of TESP used by the groups in each interval.
No start: in Interval 0 patients did not start due to various reasons; no start in Intervals 1 or 2 means that patients finished Interval 0 or 1 but did not start the next interval (1 or 2, respectively) due to dropout.
At risk: number of patients that started in the interval.
GULR dropout: patients who dropped out due to characteristics of the GULR.
Pending: subjects that are still in the middle of the interval.
Completed interval: an interval that has ended either because of TESP removal or because of death of the patient.
Completed study: patients that finished Interval 2 or died in Interval 2.
[a] Dropout due to problems with fistula ($n = 1$) and death ($n = 1$) in Interval 0.
[b] Dropout due receiving the wrong type of TESP ($n = 1$) and due to fistula problems ($n = 1$) in Interval 0.
[c] Dropout after Interval 1 due to personal reasons ($n = 1$).
[d] No more TESP usage ($n = 1$).

Table 3
Mean, median, and standard deviation of lifetime in days per interval per type of TESP, and all intervals added per type of TESP.

Type of TESP	Interval 0				Interval 1				Interval 2				Summed intervals			
	Mean	Median	SD	*N*	Mean	Median	SD	*N*	Mean	Median	SD	*N*	Mean	Median	SD	*N*
GULR	129.0	73.5	154.4	22	118.8	73.0	130.8	15	94.9	41.5	95.2	12	117.5	73.0	133.0	49
Provox2	120.1	82.5	111.6	34	135.7	84.0	155.7	29	116.2	102.5	96.7	18	124.8	84.0	125.2	81

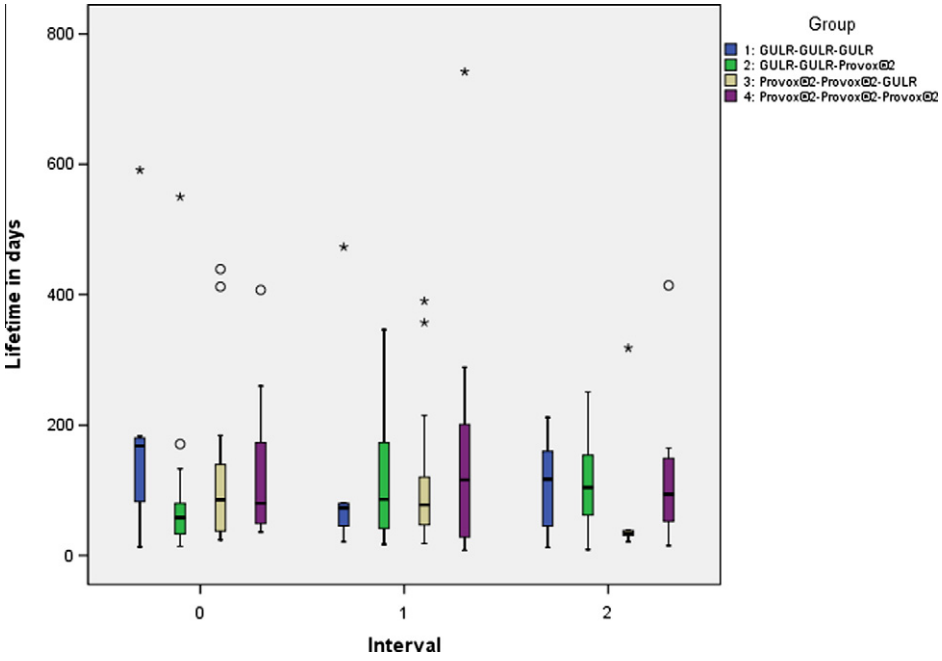

Figure 1 Lifetime in days in all intervals per group per interval. GULR is Groningen Ultra Low Resistance.

Table 4
Survey of completed subjects, dropout rates due to GULR-related reasons, and patients' preference.

Group	Interval 2 completed	Preference Provox2	Preference GULR	Dropout due to GULR	Total Provox2 preference	Total known preference
1	6[a]	1	4	8	9	13
2	6	5	1	8	13	14
3	6	3	3	5	8	11
4	12[a]	9	2	0	9	11
Total	30	18	10	21	39	49

Interval 2 completed: patients finished the study or died in Interval 2.
Preference Provox2: patients completed the study with Provox2 preference.
Preference GULR: patients completed the study with GULR preference.
Dropout due to GULR: patients that dropped out due to GULR-related reasons.
Total Provox2 preference: patients that either completed the study with Provox2 preference or dropped out due to GULR-related reasons.
Total known preference: total number of patients for whom preference is known.
[a] One subject died in Interval 2, which means the study was completed but preference was unknown.

total of 39 patients who preferred Provox2. Ten patients ended up having GULR preference. Thus 79.6% of the patients preferred using a Provox2 voice prosthesis ($P < 0.001$).

TESP replacement reasons

The number of replacements evaluated was 44 for GULR and 71 for Provox2. There are many reasons to replace a TESP. The most important replacement reasons in our study were: leakage though the TESP (GULR 59.1% and Provox2 52.1% of all replacements); HPR (GULR 15.9% and Provox2 12.7% of all replacements); and leakage around the TESP (GULR 4.6% and Provox2 4.2% of all replacements). Other less frequent replacement reasons were growth of granulation tissue around or over the TESP, or dislocation of the TESP.

Discussion

The mean device lifetimes we found were 106.2 and 102.7 days, and median lifetimes were 76 and 65 days for GULR and Provox2, respectively. These figures are consistent with the literature,[3–11] in which great variability in mean (33[3] to 147[8] days) and median (30[11] to 144[6] days) lifetime in Provox2 is shown, and also a high range with measured lifetimes varying from 7[5] to 735[6] days. The GULR lifetime results are comparable with the literature as well (mean 65[3] to >95.2 (range 14–182)[7] and median 48[3]). Even though, most of these studies had retrospective designs, in contrast to our study, our results showed the same kind of great variability.

According to our protocol, new patients were to be included in case where there were more than four dropouts per group.

However, because we considered the "dropout due to GULR" to be a result instead of normal dropout, that is, patients' preference, we decided not to replace these patients. Moreover, an ethical conflict would thus arise: Should we expose more patients to a TESP that appears unfavorable to the patient? As a result, we were able to collect less data on GULR lifetime (especially in Interval 2) than expected, which negatively influenced the power of the study. Furthermore, ending the study before all subjects had finished caused missing data in the GULR Interval 2, though for only three patients. In light of the very significant preference, the benefit of waiting for these patients to finish would not have affected the results.

Interestingly, patients' preference was highly significantly in favor of Provox2. This finding is new in literature. It suggests that other TESP aspects besides lifetime are equally as important for the patients' comfort. The main factor is the HPR seen in the high GULR-related dropout. Other factors of discomfort were "cleaning problems" "problematic replacement procedures", "sizing problems", and "increased shortness of breath" in an asthma patient. Consequently, these factors could be useful in designing a new TESP.

Our hypotheses assumed the phonating resistance of Provox2 and GULR to be comparable. However, the studies on the phonating characteristics of several TESP types, both in vitro and in vivo, unfortunately are all characterized by different methods used to measure the TESPs' aerodynamics.[7,8,11,16–18] Chung and colleagues[7] measured a mean maximum phonation time (MPT) of 16 s (range 7–42 s) one week after GULR insertion. Terada and colleagues[8] measured a mean MPT in Provox2 of 15.1 s (range 8–28 s). The timing of both these measurements with respect to the moment of insertion of the Provox2 is unclear. While the MPT in both TESPs is comparable, the high GULR dropout due to HPR was unexpected.

Strikingly, the second most important reason for dropout was TESP leakage immediately after insertion (14.3% of all dropouts). This would suggest that the TESP valve was constantly open, which could be caused by low intra-esophageal pressure or a rigid TESP in a small fistula. Some hypothesize that cold TESP temperature immediately after insertion causes additional rigidity and leakage. The immediate leakage and HPR seem contrasting, and the mechanism behind these characteristics is unclear, even more so considering the one patient who experienced both leakage and high phonation resistance at the same time.

Leakage through the TESP was the main replacement reason, which is consistent with the literature on older types of TESPs.[19] Oosterhof and colleagues[20] retrospectively compared the Groningen Low Resistance (GLR) and Provox2 replacement reasons and found higher leakage percentages in Provox2 (GLR 57% and Provox2 76%). Their percentage of leakage around the TESP was higher (14% in GLR and Provox2). HPR as replacement reason in their study was 12% (GLR and Provox2). We found a higher percentage of HPR in GULR (15.9%), which contrasts with Chung and colleagues[18] who showed a significantly lower in vitro airflow resistance in GULR compared to GLR. This suggests that HPR directly after insertion and HPR as a replacement reason are two separate entities with different origins. Biofilm formation might be of influence on "later onset" HPR, while TESP design seems to influence the HPR directly after insertion.

When reviewing our results, we found no significant differences between GULR and Provox2. However, the preference of patients for Provox2 was significant ($P < 0.001$). Therefore, we recommend Provox2 in the voice rehabilitation of post-laryngectomy patients. Since patients' preference was a leading factor in our results, we suggest that in future studies on TESP effectiveness patients' preference should be considered as an outcome measurement equally as important as the median device lifetime figure.

Conflict of interest statement

None declared.

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References

1. Blom ED, Hamaker RC. Tracheoesophageal voice restoration following total laryngectomy. In: Myers EN, Suen J, editors. *Cancer of the head and neck*. Philadelphia: WB Saunders Publishers; 1996. p. 839–52.
2. Van Weissenbruch R, Albers FW. Voice rehabilitation after total laryngectomy. *Acta Otorhinolaryngol Belg* 1992;**46**(2):221–46.
3. Schwandt LQ. Clinical aspects of postlaryngectomy voice rehabilitation, thesis 2005.
4. Op de Coul BM, Hilgers FJ, Balm AJ, Tan IB, van den Hoogen FJ, van Tinteren H. A decade of postlaryngectomy vocal rehabilitation in 318 patients: a single institution's experience with consistent application of provox indwelling voice prostheses. *Arch Otolaryngol Head Neck Surg* 2000;**126**(11):1320–8.
5. Ackerstaff AH, Hilgers FJ, Meeuwis CA, van der Velden LA, van den Hoogen FJ, Marres HA, et al. Multi-institutional assessment of the Provox 2 voice prosthesis. *Arch Otolaryngol Head Neck Surg* 1999;**125**(2):167–73.
6. Lequeux T, Badreldin A, Saussez S, Thill MP, Oujjan L, Chantrain G. A comparison of survival lifetime of the Provox and the Provox2 voice prosthesis. *J Laryngol Otol* 2003;**117**(11):875–8.
7. Chung RP, Dagli AS, Geskus J, de Bruin MD, Mahieu HF. The ultra-low resistance Groningen voice prosthesis: clinical experiences. *Rev Laryngol Otol Rhinol* 2001;**122**(2):129–33.
8. Terada T, Saeki N, Toh K, Uwa N, Sagawa K, Takayasu S, et al. Voice rehabilitation with Provox2 voice prosthesis following total laryngectomy for laryngeal and hypopharyngeal carcinoma. *Auris Nasus Larynx* 2007;**34**(1):65–71.
9. Balle VH, Rindsø L, Thomsen JC. Primary speech restoration at laryngectomy by insertion of voice prosthesis–10 years experience. *Acta Otolaryngol Suppl.* 2000;**543**:244–5.
10. Schäfer P, Klützke N, Schwerdtfeger FP. Voice Restoration with Voice Prosthesis after Total Laryngectomy. Assessment of Survival Time of 378 Provox-1, Provox-2 and Blom-Singer Voice Prosthesis. *Laryngo-Rhino-Otol* 2001;**80**(11):677–81.
11. Schwandt LQ, Tjong-Ayong HJ, van Weissenbruch R, van der Mei HC, Albers FW. Differences in aerodynamic characteristics of new and dysfunctional Provox 2 voice prostheses in vivo. *Eur Arch Otorhinolaryngol* 2006;**263**(6):518–23.
12. Elving GJ, van der Mei HC, Busscher HJ, van Weissenbruch R, Albers FW. Comparison of the microbial composition of voice prosthesis biofilms from patients requiring frequent versus infrequent replacement. *Ann Otol Rhinol Laryngol* 2002;**111**(3 Pt 1):200–3.
13. Oozeer NB, Owen S, Perez BZ, Jones G, Welch AR, Paleri V. Functional status after total laryngectomy: cross-sectional survey of 79 laryngectomees using the Performance Status Scale for Head and Neck Cancer. *J Laryngol Otol* 2010;**124**(4):412–6.
14. Schrijvers ML, van Riel EL, Langendijk JA, Dikkers FG, Schuuring E, van der Wal JE, et al. Higher laryngeal preservation rate after CO2 laser surgery compared with radiotherapy in T1a glottic laryngeal carcinoma. *Head Neck* 2009;**31**(6):759–64.
15. Papadas TA, Alexopoulos EC, Mallis A, Jelastopulu E, Mastronikolis NS, Goumas P. Survival after laryngectomy: a review of 133 patients with laryngeal carcinoma. University Hospital of Patras, Patras, Greece. *Eur Arch Otorhinolaryngol* 2010;**267**(7):1095–101.
16. Chung RP, Patel P, Ter Keurs M, Van Lith Bijl JT, Mahieu HF. In vitro and in vivo comparison of the low-resistance Groningen and the Provox tracheosophageal voice prostheses. *Rev Laryngol Otol Rhinol* 1998;**119**(5):301–6.
17. Grolman W, Eerenstein SE, Tan FM, Tange RA, Schouwenburg PF. Aerodynamic and sound intensity measurements in tracheoesophageal voice. *J Otorhinolaryngol Relat Spec* 2007;**69**(2):68–76.
18. Chung RP, Geskus J, Mahieu HF. The ultra-low resistance Groningen voice prosthesis: aerodynamic properties. *Rev Laryngol Otol Rhinol* 1999;**120**(4):245–8.
19. Van den Hoogen FJA, Oudes MJ, Hombergen G, Nijdam HF, Manni JJ. The Groningen, Nijdam and Provox voice prostheses. A prospective clinical comparison based on 845 replacements. *Acta Otolaryngol* 1996;**116**:119–24.
20. Oosterhof JJ, van der Mei HC, Busscher HJ, Free RH, Kaper HJ, van Weissenbruch R, et al. In vitro leakage susceptibility of tracheoesophageal shunt prostheses in the absence and presence of a biofilm. *J Biomed Mater Res B Appl Biomater* 2005;**73**(1):23–8.